AP Valves 2019
Seoul, Korea, Aug 9-11, 2019

Current Status of TAVR
What We Have Achieved

Horst Sievert, Eberhard Grube

Kolja Sievert, Ilona Hofmann, Sameer Gafoor, Stefan Bertog, Predrag Matić, Markus Reinartz, Bojan Jovanovic, Shahrak Zaker, Iris Grunwald, Nalan Schnelle, Robert Andel

CardioVascular Center Frankfurt - CVC,

Frankfurt, Germany

Disclosures

Physician name	Company	Relationship
Horst Sievert	4tech Cardio, Abbott, Ablative Solutions, Ancora Heart, Append Medical, Bavaria Medizin Technologie GmbH, Bioventrix, Boston Scientific, Carag, Cardiac Dimensions, Cardimed, Celonova, Comed B.V., Contego, CVRx, Dinova, Edwards, Endologix, Hemoteq, Hangzhou Nuomao Medtech, Holistick Medical, Lifetech, Maquet Getinge Group, Medtronic, Mokita, Occlutech, Recor, Renal Guard, Terumo, Vascular Dynamics, Vectorious Medtech, Venock, Venus, Vivasure Medical	Study honoraria to institution, travel expenses, consulting fees to institution

Valvular heart interventions started as early as 1953

Rubio-Alvarez developed the first transcatheter valve intervention

Scroll saw for treatment of pulmonary valve stenosis

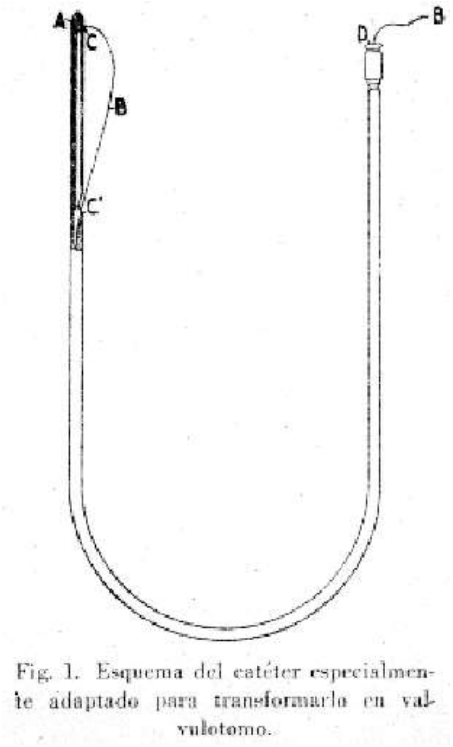


Fig. 1. Esquema del catéter especialmente adaptado para transformarlo en valvulotomo.

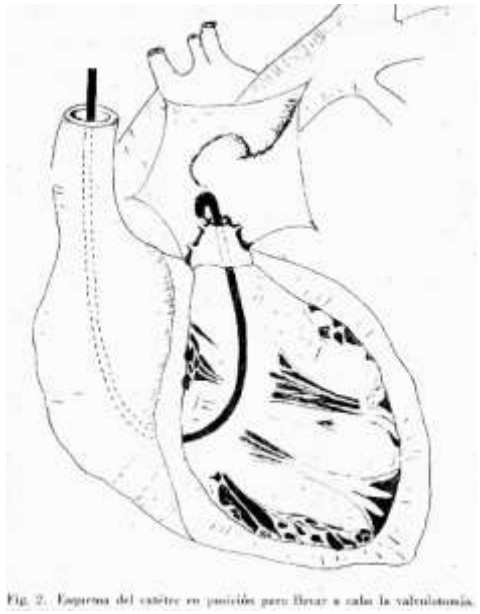
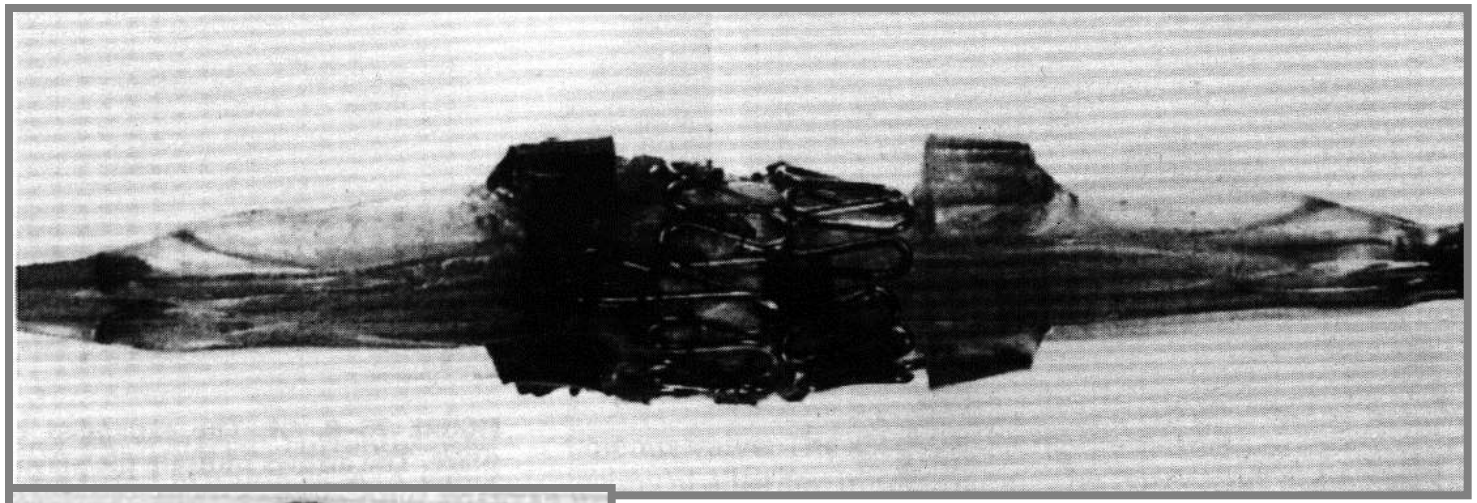


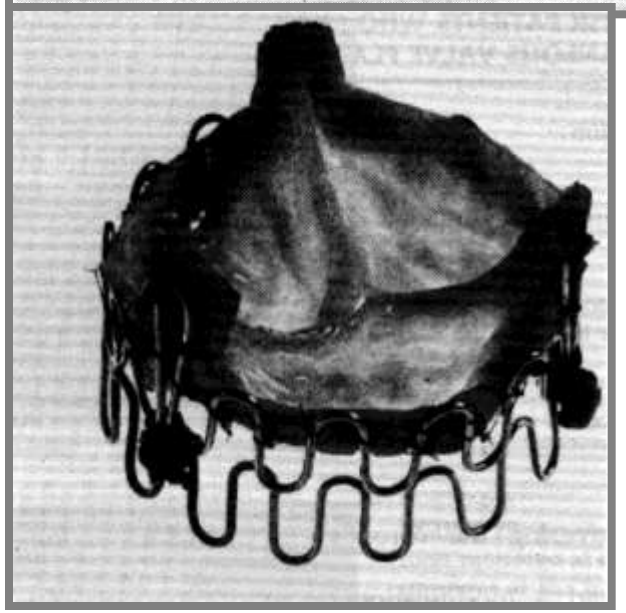
Fig. 2. Esquema del catéter en posición para llevar a cabo la valvulotomía.

It took 50 years from the scroll saw
to the first transcatheter valve implantations ....

Rubio-Alvarez V, Arch Inst Cardiol Mex. 1953 Apr;23(2):183-92

Andersen- Valve (1992)



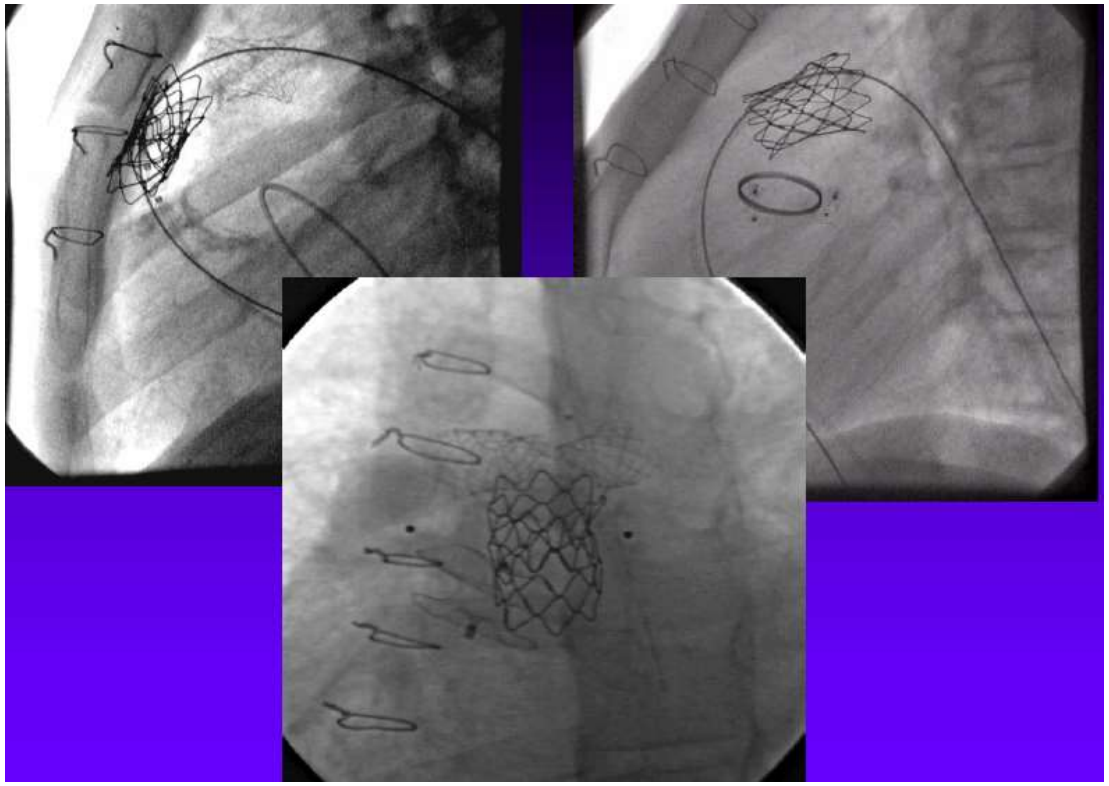


- In bench models and in animals
- Implantation into the descending and ascending aorta

Andersen HR, Eur Heart J 1992

Bonhoeffer, Oct. 2000
First percutaneous valve implantation

Bovine venous valve
Balloon expandable stent



Implanted into a pulmonary homograft

Bonhoeffer et al, JAAC 2002

Alain Cribier: First Transcatheter Aortic Valve Implantation (TAVI) April 16, 2002

April 16, 2002

8 days post implantation

First Transcatheter Aortic Valve Implantation, April 16, 2002

Within the last 10 years >70 new percutaneous valves and valve repair techniques have been developed

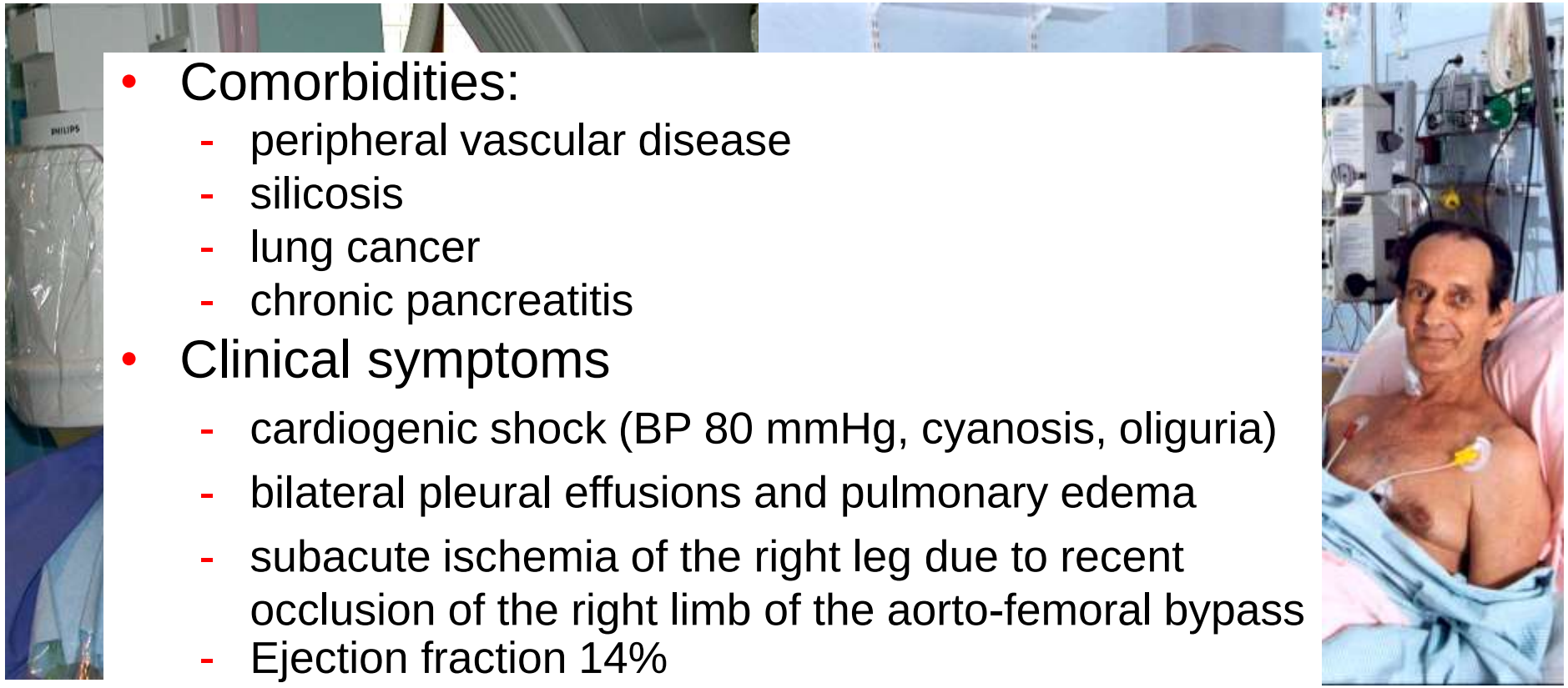
There was a major and fundamental difference in how TAVR developed compared to other interventions

Most other cardiovascular interventions were initially used in relatively healthy patients

• 1921	Heart catheterization	Werner Forßmann (self experiment)
• 1960	Surgical valve replacement	52 y/o patient without co-morbidities
• 1967	CABG	51 y/o female patient w/o co-morbidities
• 1974	Transcatheter ASD closure:	17 y/o otherwise healthy girl
• 1977	PCI	38 y/o patient, very low surgical risk
• 2003	First MitraClip	55 y/o healthy woman

In TAVR, the approach was the other way around

Alain Cribier: First TAVI April 16, 2002



- Comorbidities:
  - peripheral vascular disease
  - silicosis
  - lung cancer
  - chronic pancreatitis
- Clinical symptoms
  - cardiogenic shock (BP 80 mmHg, cyanosis, oliguria)
  - bilateral pleural effusions and pulmonary edema
  - subacute ischemia of the right leg due to recent occlusion of the right limb of the aorto-femoral bypass
  - Ejection fraction 14%
- Turned down by several cardiac surgical teams

In the early days of TAVR …

… we showed more slides about comorbidities, risk factors and complications than about results of the procedure

Today

- TAVR has become a routine procedure in many cath-labs around the world
- Local anesthesia
- Less than 1 hour
- Mortality < 1%

TAVR with Sapien and Evolut have proven success in extreme, high, and intermediate risk patients

Extreme Risk → **High Risk** → **Intermediate Risk**

The NEW ENGLAND JOURNAL of MEDICINE

OCTOBER 21, 2010

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery

Jeffrey J. Popma, M.D.,* David H. Adams, M.D.,† Michael J. Reardon, M.D.,† Steven J. Yakubov, M.D.,† Neal S. Kleiman, M.D.,‡ David Heimansohn, M.D.,§ James Hermiller, Jr., M.D.,‖ G. Chad Hughes, M.D.,¶ J. Kevin Harrison, M.D.,¶ Joseph Coselli, M.D.,# Jose Diez, M.D.,# Ali Kafi, M.D.,** Theodore Schreiber, M.D.,** Thomas G. Gleason, M.D.,†† John Conte, M.D.,‡‡ Maurice Buchbinder, M.D.,§§ G. Michael Deeb, M.D.,§§ Blasé Carabello, M.D.,¶¶ Patrick W. Serruys, M.D., PhD,## Sharla Chenoweth, M.S.,*** Jae K. Oh, M.D.,††† for the CoreValve United States Clinical Investigators

Boston, Massachusetts; New York, New York; Houston, Texas; Columbus, Ohio; Indianapolis, Indiana; Durham, North Carolina; Detroit and Ann Arbor, Michigan; Pittsburgh, Pennsylvania; Baltimore, Maryland; Palo Alto, California; Rotterdam, the Netherlands; and Minneapolis and Rochester, Minnesota

The NEW ENGLAND JOURNAL of MEDICINE

JUNE 9, 2011

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D., Steven J. Yakubov, M.D., Joseph S. Coselli, M.D., G. Michael Deeb, M.D., Thomas G. Gleason, M.D., Maurice Buchbinder, M.D., James Hermiller, Jr., M.D., Neal S. Kleiman, M.D., Stan Chetcuti, M.D., John Heiser, M.D., William Merhi, D.O., George Zorn, M.D., Peter Tadros, M.D., Newell Robinson, M.D., George Petrossian, M.D., G. Chad Hughes, M.D., J. Kevin Harrison, M.D., John Conte, M.D., Brijeshwar Maini, M.D., Mubashir Mumtaz, M.D., Sharla Chenoweth, M.S., and Jae K. Oh, M.D., for the U.S. CoreValve Clinical Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

M.J. Reardon, N.M. Van Mieghem, J.J. Popma, N.S. Kleiman, L. Søndergaard, M. Mumtaz, D.H. Adams, G.M. Deeb, B. Maini, H. Gada, S. Chetcuti, T. Gleason, J. Heiser, R. Lange, W. Merhi, J.K. Oh, P.S. Olsen, N. Piazza, M. Williams, S. Windecker, S.J. Yakubov, E. Grube, R. Makkar, J.S. Lee, J. Conte, E. Vang, H. Nguyen, Y. Chang, A.S. Mugglin, P.W.J.C. Serruys, and A.P. Kappetein, for the SURTAVI Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

TAVR in low surgical risk?

This discussion is over!

PARTNER 3 Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

EVOLUT Low Risk Trial

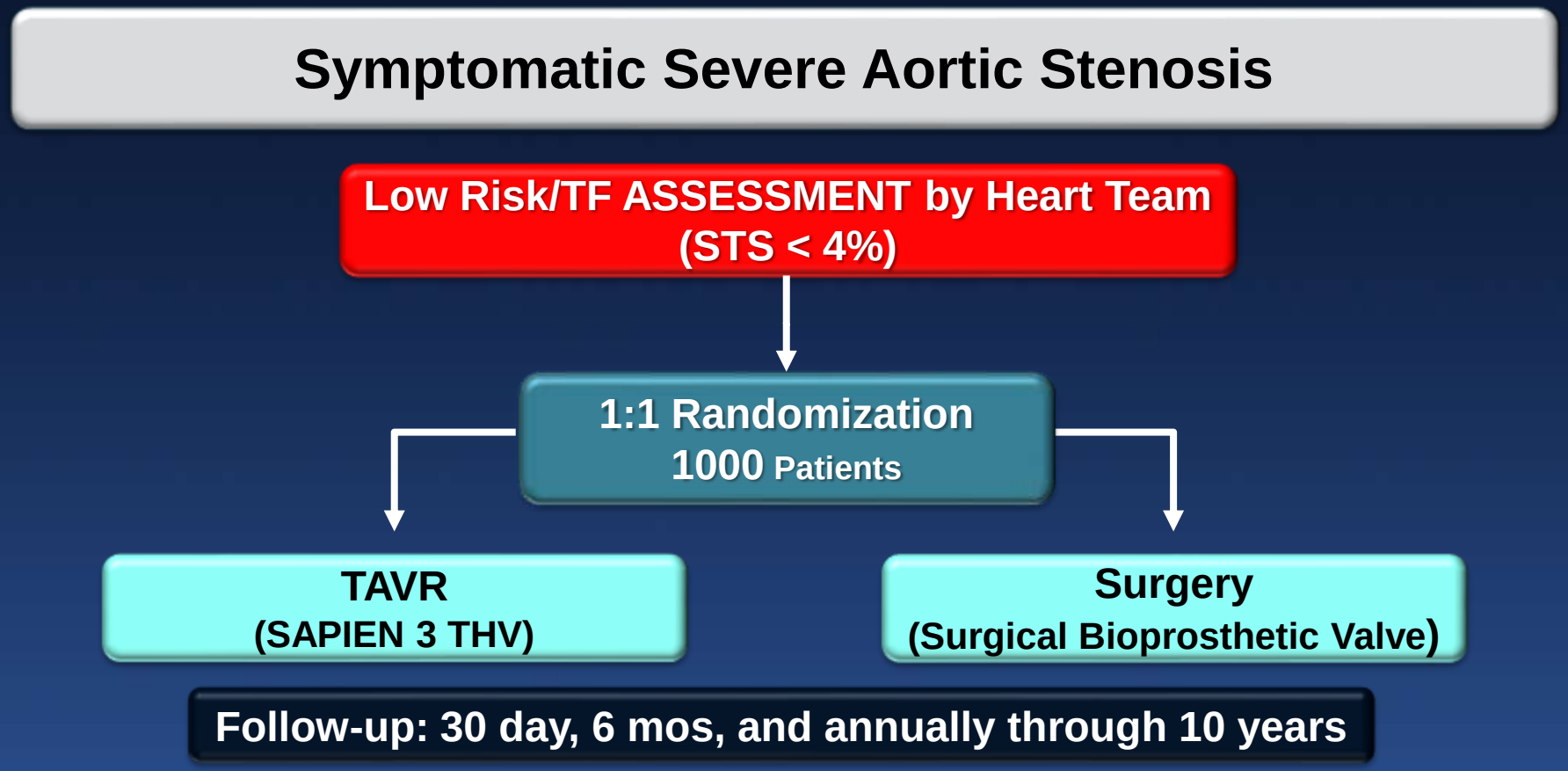
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, obinson, M.D., George Petr K. Oh, M.D., Michael J. Boul . Mugglin, Ph.D., and Michael J. Investigators*

PARTNER 3 Study Design



PRIMARY ENDPOINT:
Composite of all-cause mortality, stroke, or CV re-hospitalization at 1 year post-procedure

M Leon, ACC 2019

Procedural & Hospital Findings

THE PARTNER 3 TRIAL

All differences in favor of TAVR

% or mean ± SD

Variable	TAVR (N=496)	Surgery (N=454)	P-value
Conscious Sedation	65.1%	NA	NA
Procedure Time (min)	58.6 ± 36.5	208.3 ± 62.2	<0.001
Fluoroscopy Time (min)	13.9 ± 7.1	NA	NA
Aortic Cross-Clamp Time (min)	NA	74.3 ± 27.8	NA
Total CPB Time (min)	NA	97.7 ± 33.8	NA
Median ICU Stay (days)	2.0	3.0	<0.001
Median Total LOS (days)	3.0	7.0	<0.001
Discharge to Home/Self-care	96.0%	73.1%	<0.001
Concomitant Procedures	7.9%	26.4%	<0.001

M Leon, ACC 2019

Procedural Complications

In-Hospital

Differences not significant but **all** are in favor of TAVR

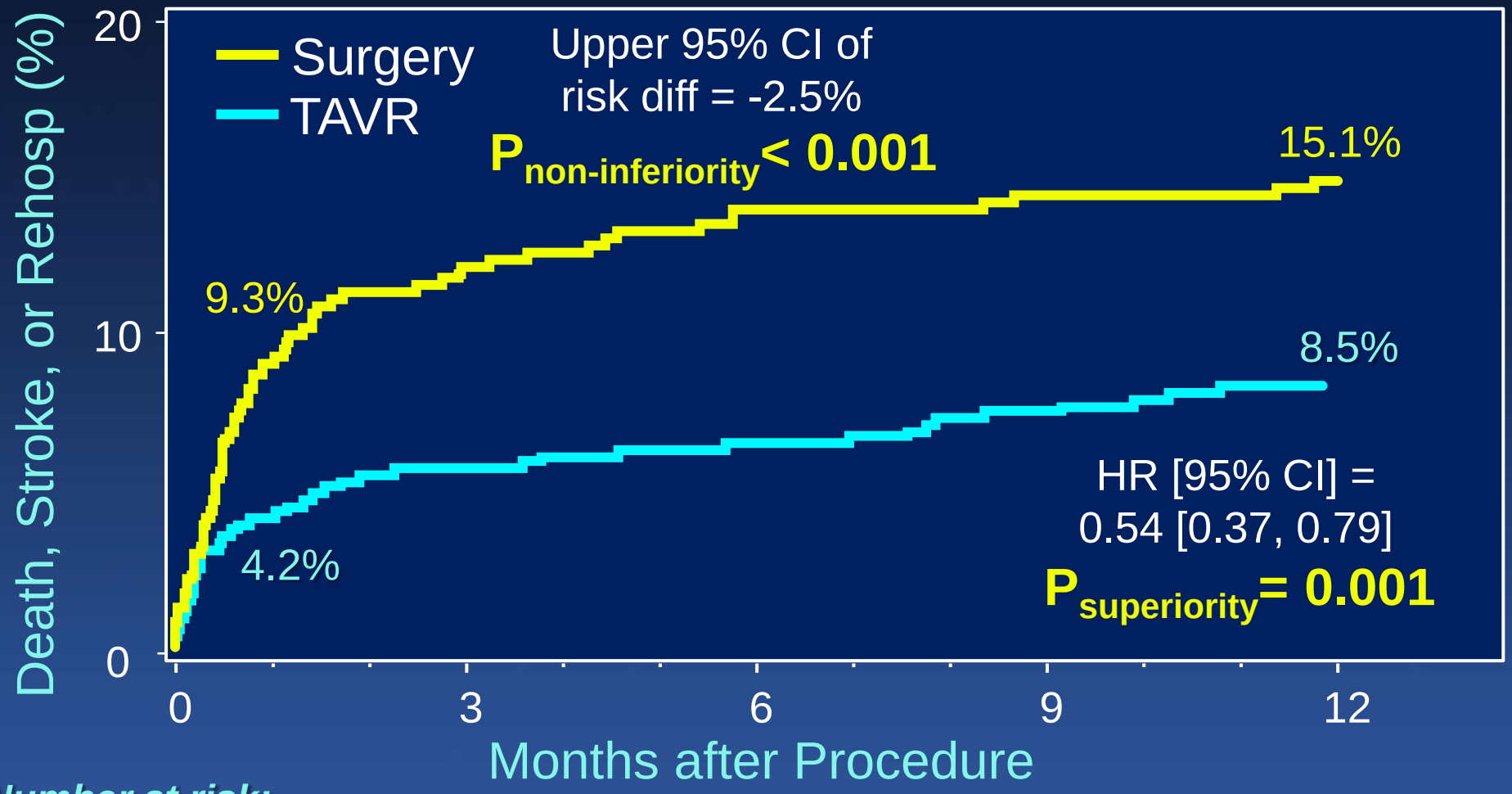
% or mean ± SD

Complication	TAVR (N=496)	Surgery (N=454)	P-value
In-hospital Death	0.4% (2)	0.9% (4)	0.43
≥ 2 Transcatheter Valves Implanted*	0.2% (1)	NA	NA
Valve Embolization	0	NA	NA
Aortic Dissection	0	NA	NA
Annular Rupture	0.2% (1)	NA	NA
Ventricular Perforation	0.2% (1)	0.4% (2)	0.61
Coronary Obstruction	0.2% (1)	0.4% (2)	0.61
Access Site Infections	0.4% (2)	1.3% (6)	0.16

*Valve-in-valve

Primary Endpoint

All-cause mortality, all strokes, or CV re-hospitalization at 1 year



Number at risk:

Surgery	**454**	**408**	**390**	**381**	**377**	**374**
TAVR	**496**	**475**	**467**	**462**	**456**	**451**

THE PARTNER 3 TRIAL

Pre-specified Secondary Endpoints

Subject to Multiplicity Adjustment

Order of Testing	Endpoint	TAVR (N=496)	Surgery (N=454)	Treatment Effect [95% CI]	P-value
1	New onset atrial fibrillation at 30 days	5.0%	39.5%	0.10 [0.06, 0.16]	<0.001
2	Length of index hospitalization (days)	3.0 (2.0, 3.0)	7.0 (6.0, 8.0)	-4.0 [-4.0, -3.0]	<0.001
3	All-cause death, all stroke, or rehospitalizations at 1 year	8.5%	15.1%	0.54 [0.37, 0.79]	0.001
4	Death, KCCQ < 45 or KCCQ decrease from baseline ≥ 10 points at 30 days	3.9%	30.6%	-26.7% [-31.4%, -22.1%]	<0.001
5	Death or all stroke at 30 days	1.0%	3.3%	0.30 [0.11, 0.83]	0.01
6	All stroke at 30 days	0.6%	2.4%	0.25 [0.07, 0.88]	0.02

* P-value is Log-Rank test for items 1, 3, 5 and 6; P-value is Wilcoxon Rank-Sum Test for item 2; P-value is Fisher's Exact test for item 4

M Leon, ACC 2019

THE PARTNER 3 TRIAL

Other Secondary Endpoints

Outcomes	30 Days			1 Year		
	TAVR (N=496)	Surgery (N=454)	P-value	TAVR (N=496)	Surgery (N=454)	P-value
Bleeding - Life-threat/Major	3.6% (18)	24.5% (111)	<0.001	7.7% (38)	25.9% (117)	<0.001
Major Vascular Complics	2.2% (11)	1.5% (7)	0.45	2.8% (14)	1.5% (7)	0.19
AKI - stage 2 or 3*	0.4% (2)	1.8% (8)	0.05	0.4% (2)	1.8% (8)	0.05
New PPM (incl baseline)	6.5% (32)	4.0% (18)	0.09	7.3% (36)	5.4% (24)	0.21
New LBBB	22.0% (106)	8.0% (35)	<0.001	23.7% (114)	8.0% (35)	<0.001
Coronary Obstruction	0.2% (1)	0.7% (3)	0.28	0.2% (1)	0.7% (3)	0.28
AV Re-intervention	0% (0)	0% (0)	NA	0.6% (3)	0.5% (2)	0.76
Endocarditis	0% (0)	0.2% (1)	0.29			
Asymp Valve Thrombosis	0.2% (1)	0% (0)	0.34			

Most not different or in favor of TAVR except LBBB

Event rates are KM estimates (%) and p-values are based on Log-Rank test

* Event rates are incidence rates and p-value is Fisher's Exact test

Echocardiography Findings

Mean Gradient

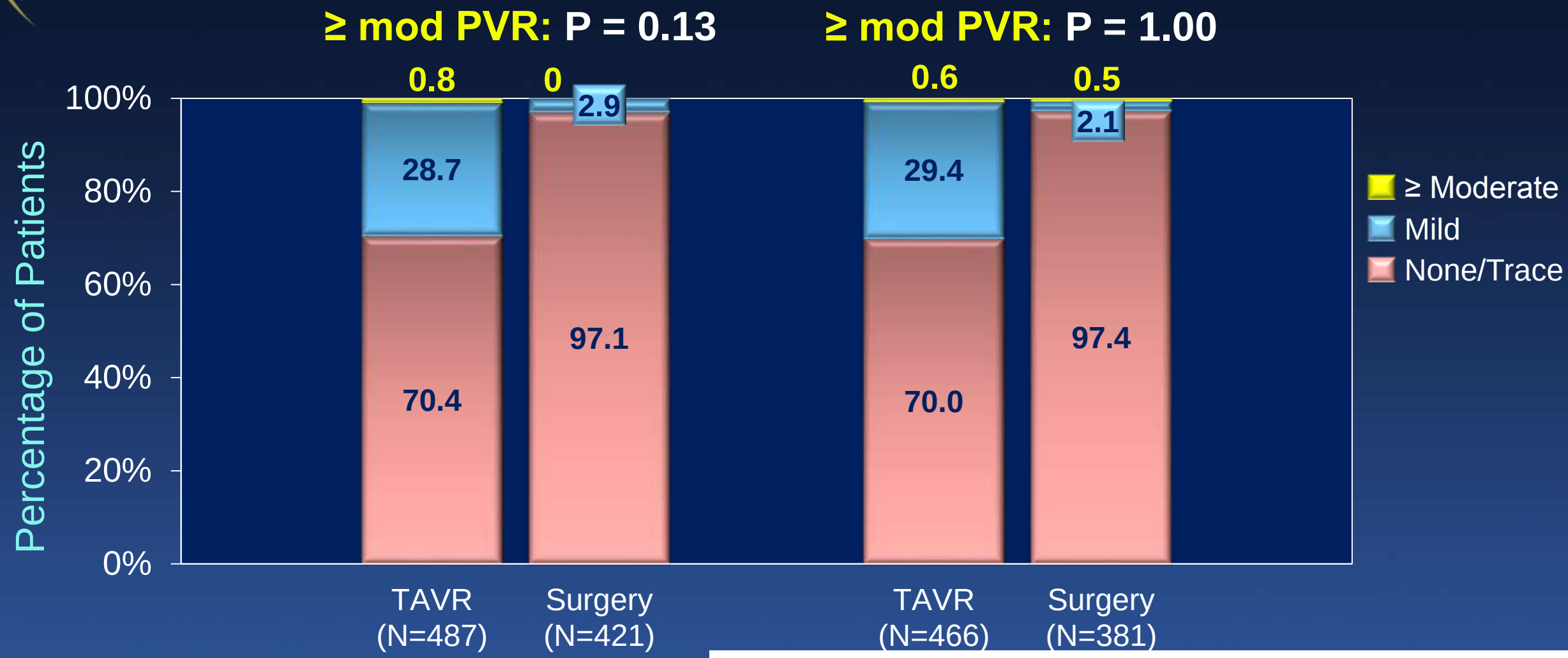
No. of Echos		
Surgery	**441**	**426**
TAVR	**483**	**490**

Significant but small difference in favor of Surgery

P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

M Leon, ACC 2019

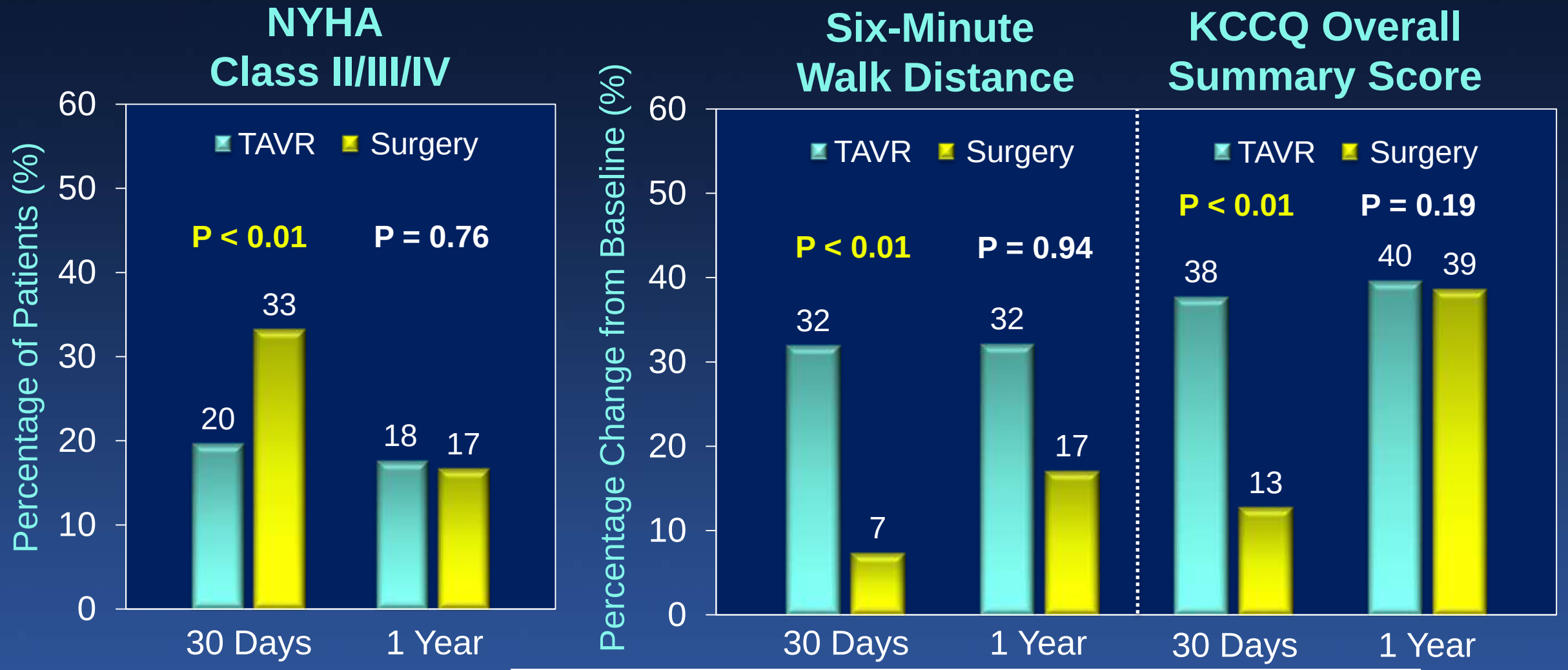
Paravalvular Regurgitation



P-values are based on the Wilcoxon rank-sum test.

Less paravalvular leaks after surgery
But most leaks are only mild

Functional Assessments



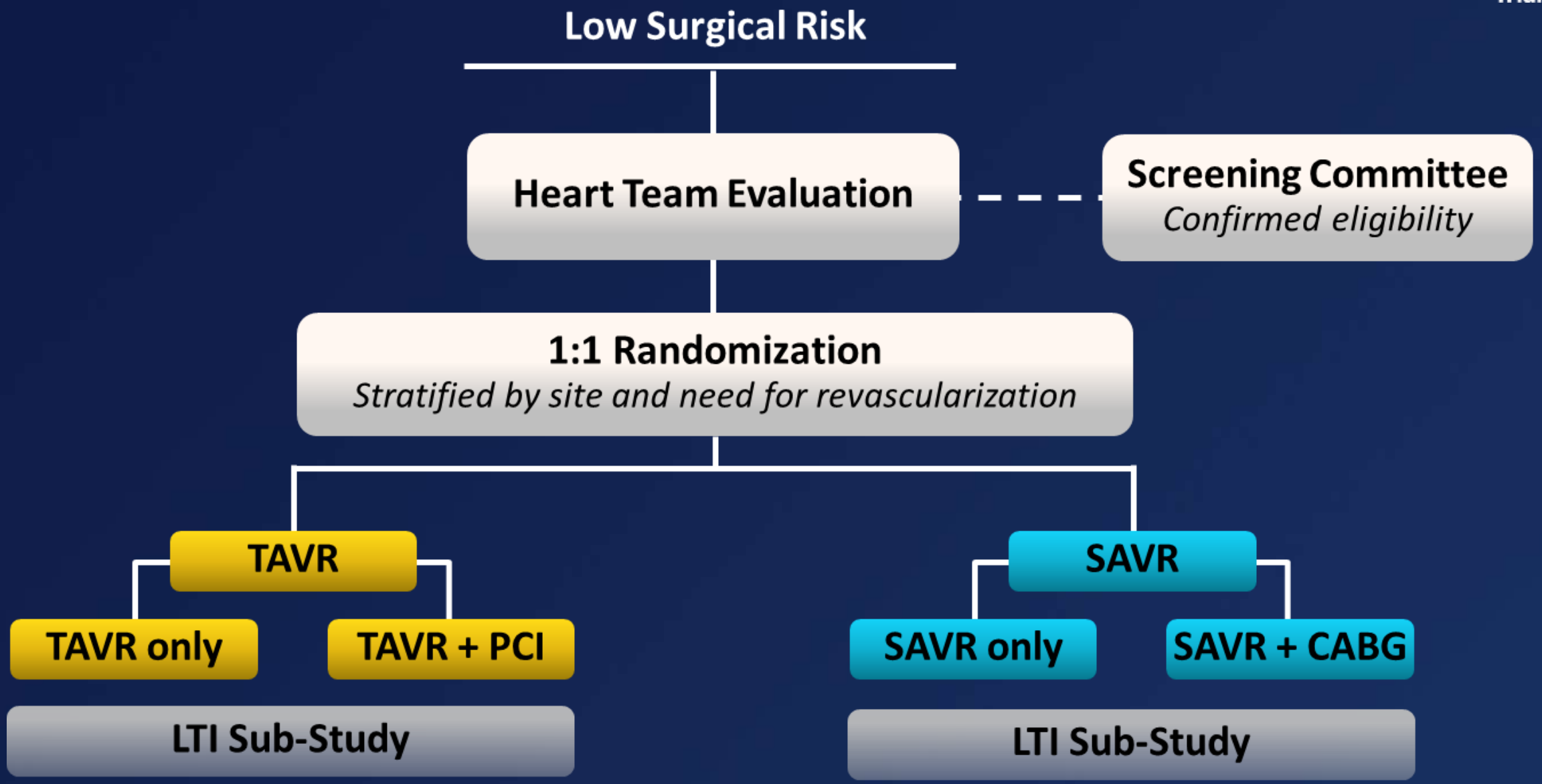
Of course patients feel better after TAVR!

P-values are based on Fisher's Exact test.

P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

And CoreValve Evolut?

Evolut Low Risk Trial Study Design

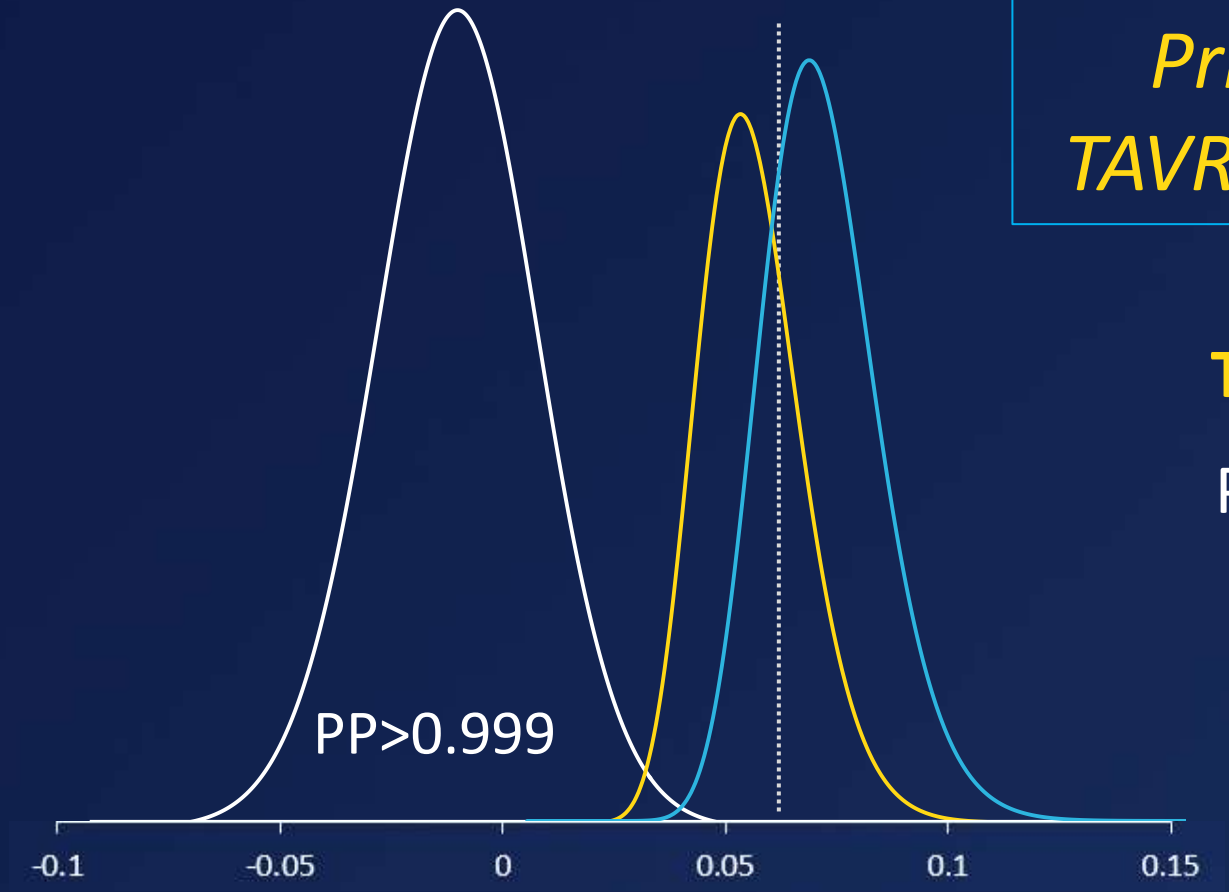


MJ. Reardon, ACC 2019

Primary Endpoint

All-Cause Mortality or Disabling Stroke at 2 Years

Evolut™ Low Risk Trial



Primary Endpoint Met
TAVR is noninferior to SAVR

TAVR 5.3% **SAVR 6.7%**

Posterior probability of noninferiority > 0.999

TAVR –SAVR difference = -1.4% (95% BCI; -4.9, 2.1)

MJ. Reardon, ACC 2019

Hierarchical Secondary Endpoints

All Noninferiority and Superiority Endpoints Met

Evolut™ Low Risk Trial

	TAVR	SAVR	Difference TAVR–SAVR	Posterior Probability
Noninferiority (margin)			(90% BCI)	
Mean gradient at 12 months (5 mmHg)	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.1, -2.1)	> 0.999 ✓
Mean EOA at 12 months (0.1 cm^2)	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	> 0.999 ✓
Mean NYHA class change (12 months –Baseline) (0.375)	0.9 ± 0.7	1.0 ± 0.7	-0.1 (-0.2, 0.0)	> 0.999 ✓
Mean KCCQ change (12 months –Baseline) (5)	22.2 ± 20.3	20.9 ± 21.0	1.3 (-1.2, 3.8)	> 0.999 ✓
Superiority			(95% BCI)	
Mean gradient at 12 months, mmHg	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.2, -2.0)	> 0.999 ✓
Mean EOA at 12 months, cm^2	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	> 0.999 ✓
Mean KCCQ change (30 Days–Baseline)	20.0 ± 21.1	9.1 ± 22.3	10.9 (8.6, 13.2)	> 0.999 ✓

MJ. Reardon, ACC 2019

Clinical Outcomes at 30 Days

Most parameters in favor of TAVR

Trial

Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
30-Day composite safety endpoint*	5.3	10.7	(-8.3, -2.6)
All-cause mortality	0.5	1.3	(-1.9, 0.2)
Disabling stroke*	0.5	1.7	(-2.4, -0.2)
Life-threatening or disabling bleeding*	2.4	7.5	(-7.5, -2.9)
Acute kidney injury, stage 2-3*	0.9	2.8	(-3.4, -0.5)
Major vascular complication	3.8	3.2	(-1.4, 2.5)
Atrial fibrillation*	7.7	35.4	(-31.8, -23.6)
Permanent pacemaker implant*	17.4	6.1	(8.0, 14.7)
All-cause mortality or disabling stroke*	0.8	2.6	(-3.2, -0.5)
All stroke	3.4	3.4	(-1.9, 1.9)
Aortic valve reintervention	0.4	0.4	(-0.8, 0.7)

* Significantly favors TAVR; * Significantly favors SAVR

BCI = Bayesian credible interval

Clinical Outcomes at 1 Year

All parameters no difference or in favor of TAVR

Evolut™ Low Risk Trial

Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
All-cause mortality or disabling stroke	2.9	4.6	(-4.0, 0.4)
All-cause mortality	2.4	3.0	(-2.6, 1.3)
Cardiovascular mortality	1.7	2.6	(-2.7, 0.7)
All stroke	4.1	4.3	(-2.4, 1.9)
Disabling stroke*	0.8	2.4	(-3.1, -0.3)
Transient ischemia attack	1.7	1.8	(-1.6, 1.3)
Myocardial infarction	1.7	1.6	(-1.3, 1.5)
Endocarditis	0.2	0.4	(-0.9, 0.5)
Valve thrombosis	0.2	0.3	(-0.9, 0.5)
Aortic valve reintervention	0.7	0.6	(-1.0, 0.9)
Heart failure hospitalization*	3.2	6.5	(-5.9, -1.0)

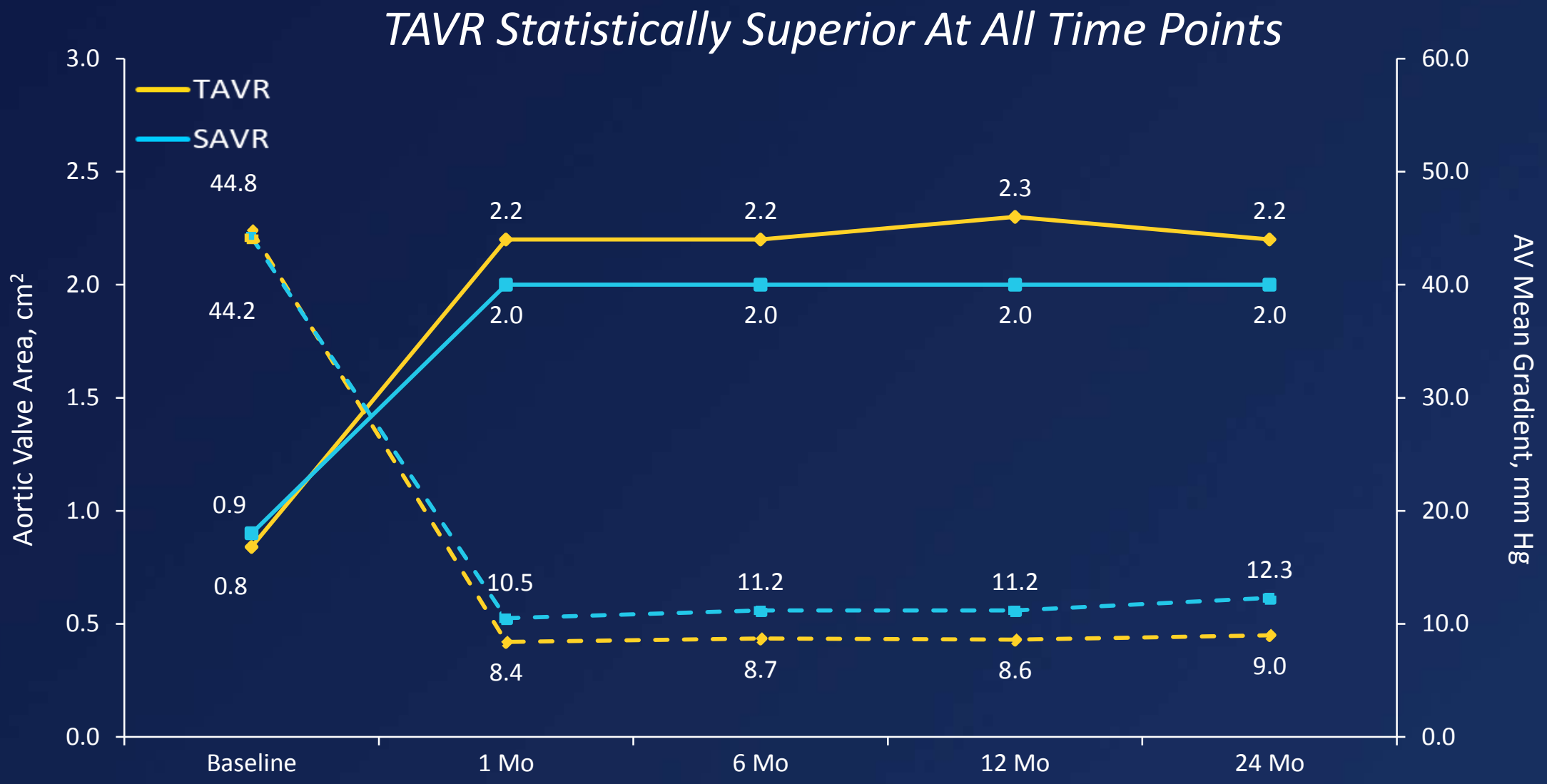
* Significantly favors TAVR

BCI = Bayesian credible interval

Valve Hemodynamics

Better hemodynamics due to supra-annular design

Evolut™ Low Risk Trial

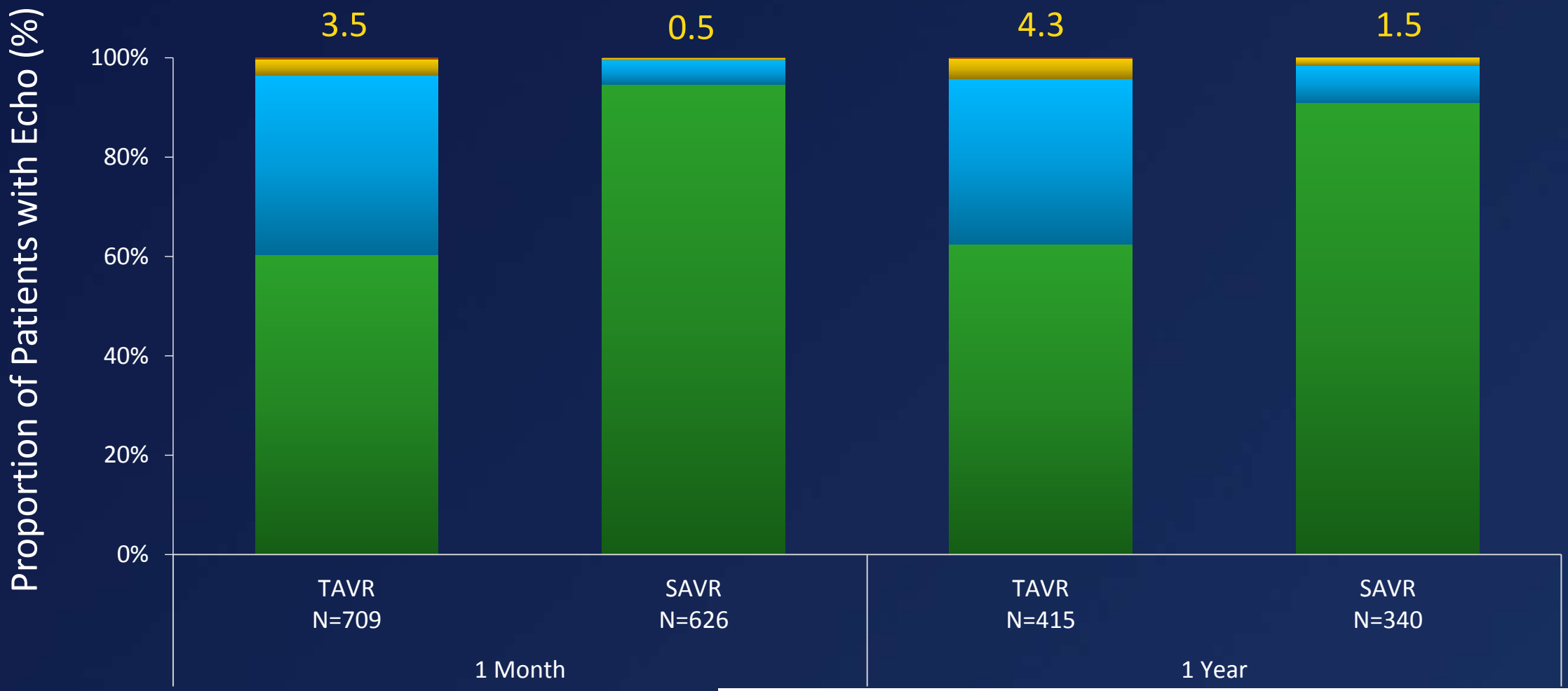


Implanted population. Core lab assessments.

MJ. Reardon, ACC 2019

Total Aortic Valve Regurgitation

Evolut™ Low Risk Trial



Less paravalvular leaks after surgery
But most leaks are only mild

MJ. Reardon, ACC 2019

Many new TAVI valves have been developed

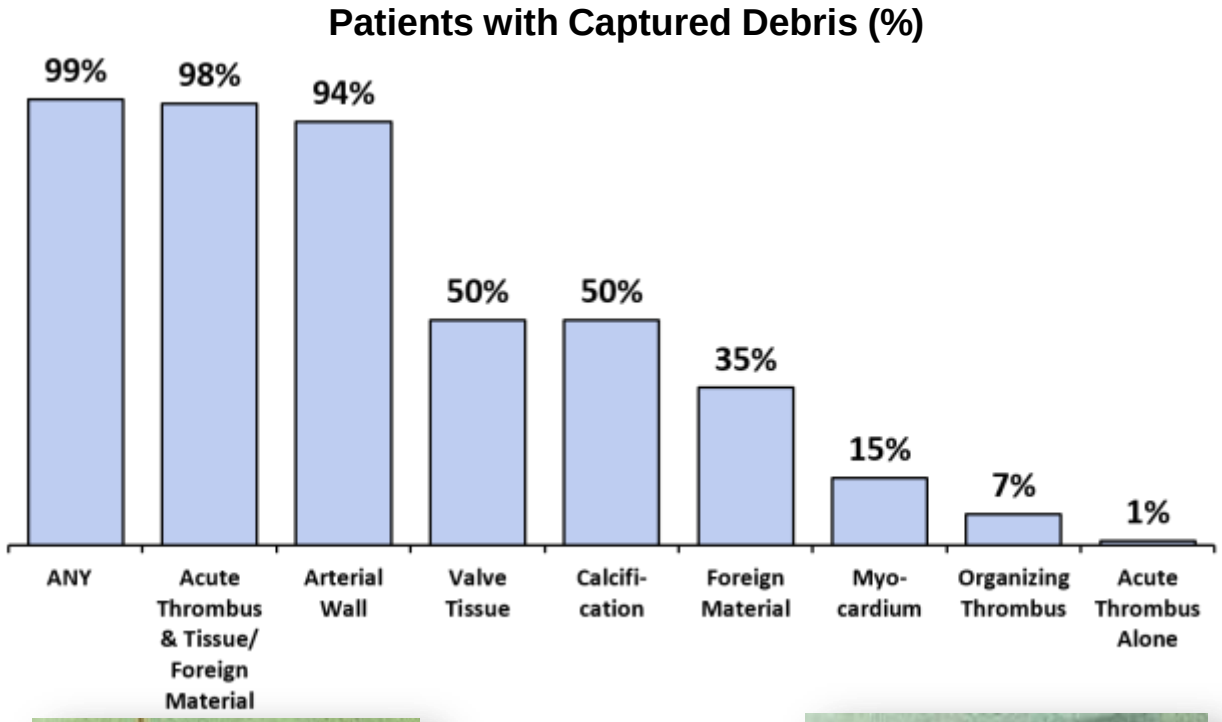
- Sapien 3
- Evolut R and Pro
- Lotus
- Acurate
- Portico
- Direct Flow
- Engager
- Jena Valve
- Centera
- Venus A Valve
- J – Valve
- NVT

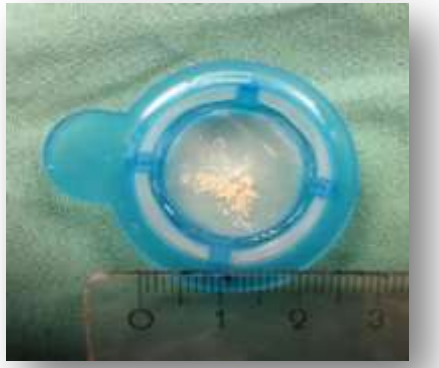
- Venibri
- VitaFlow (Microport)
- Taurus One
- Trinity
- Colibri
- Inovare
- Thubrikar
- Valve Medical
- Triskele
- BioValve (Biotronik)
- MyVal (Meril Lifescience)
- HLT Meridian
- Xeltis
- Zurich TEHV

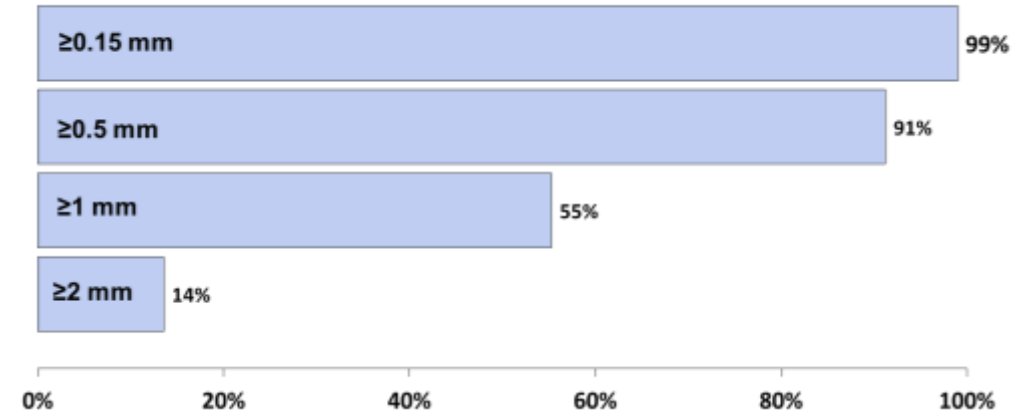
Emboli protection devices

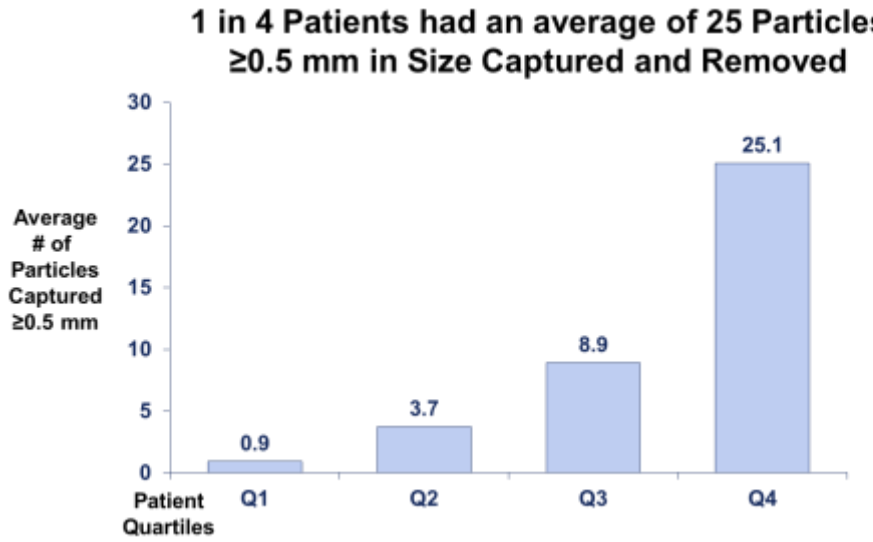
Company and Product	Claret Medical Sentinel 	Keystone TriGuard 	Edwards Embrella 	ICS Emblok 	Transverse Point-Guard 	Protembis ProtEmbo 
EU Status	CE Mark	CE Mark	CE Mark	FIM first clinical case March 15, 2017	Pre-clinical/ prototype	Pre-clinical/ prototype
US Status	• SENTINEL IDE completed 2016 • Positive FDA Panel - Feb 23, 2017 • **FDA Cleared - June 2017**	REFLECT IDE trial halted Aug 2017. Planning next trial (TRIFLECT)	No IDE yet	No IDE yet	No IDE yet	No IDE yet
Access	6 Fr Right Radial	9Fr TF	Right Radial	12Fr TF sheath	TF	6F TR
Debris	Captures and removes	Deflects downstream	Deflects downstream	Captures and removes	Deflects downstream	Deflects downstream
Placement and Interaction with TAVR devices	Not in aortic arch, minimizing device interaction	Sits in aortic arch. Devices must pass over and back across	Sits in aortic arch. Devices must pass over and back across	Deployed in ascending aorta. Does not protect during valve delivery and retrieval	Sits in aortic arch. Devices must pass over and back across	Sits in aortic arch. Devices must pass over and back across

Sentinel™ captured debris in 99% of TAVI patients







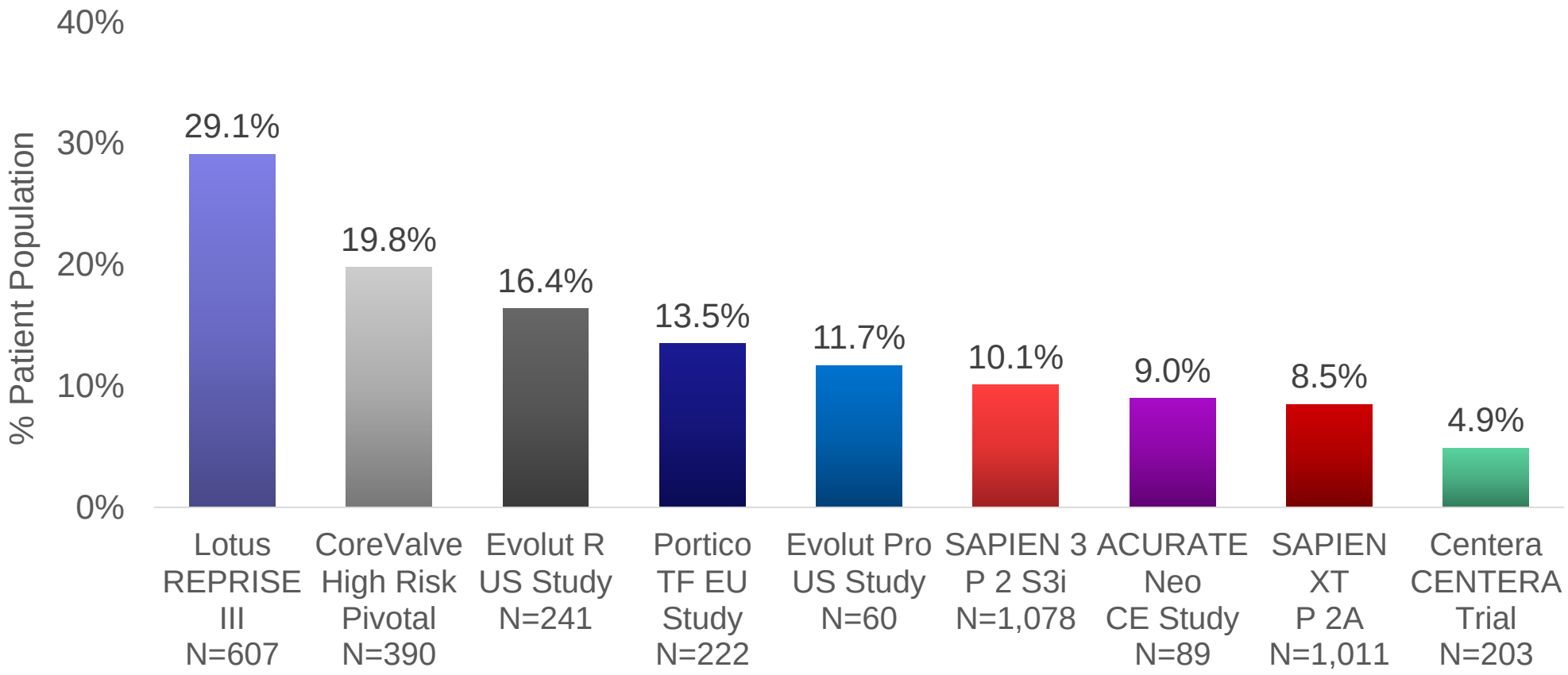


Virmani R, et al. CVPath. SENTINEL trial. Data presented at Sentinel FDA Advisory Panel, February 23, 2017

Permanent Pacemakers rates in newer TAVI valves are decreasing

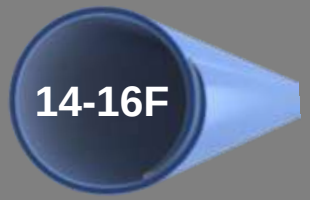
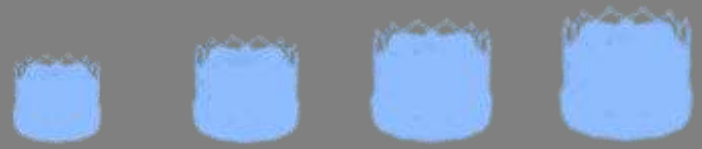
With the exception of some valve types

Rates at 30 Days



[1]Feldman, et. al. presented at EuroPCR 2017; [2]Adams, et al., *N Engl J Med* 2014;370:1790-8; [3]Popma, et al., *J Am Coll Cardiol Intv* 2017;10:268-75; [4] Mollmann, et al., *J Am Coll Cardiol Intv* 2017;10:1538-47; [5]Kodali, et al., *Eur Heart J* 2016;37:2252-62; [6]Mollmann, et al., *EuroIntervention* 2017; epub; [7]Leon, et al., *N Engl J Med* 2016;374:1609-20; [8]Tchetche, et al., presented at EuroPCR 2017; [9]Forrest, presented at TCT 2017

SAPIEN Valve Evolution

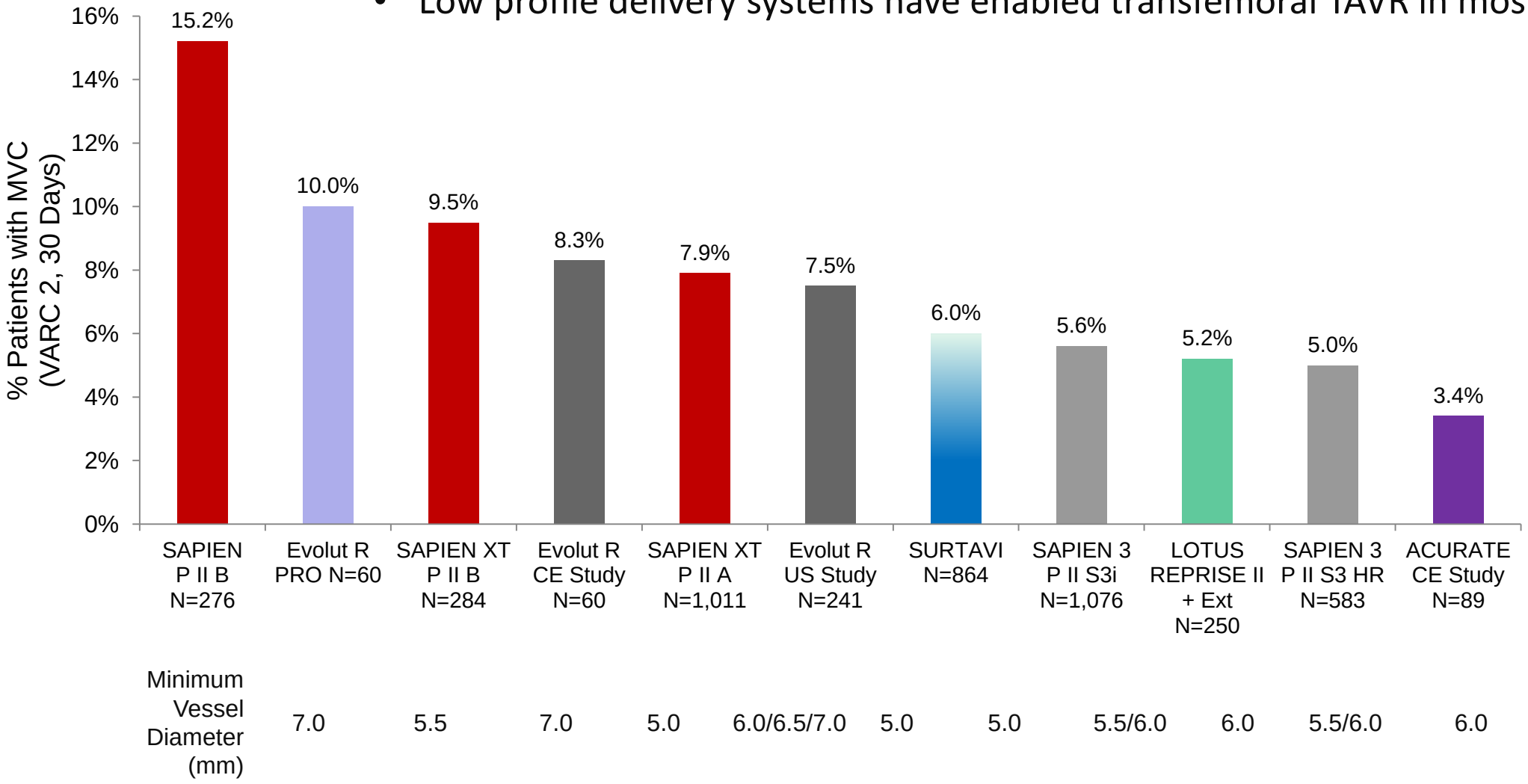
	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility			
Available Valve Sizes	 23 mm, 26 mm	 23 mm, 26 mm, 29 mm	 20 mm, 23 mm, 26 mm, 29 mm
FDA Approval of Valve:	**PARTNER 1** 2011	**PARTNER 2** 2014	**PARTNER 3** 2015

M Leon, ACC 2019

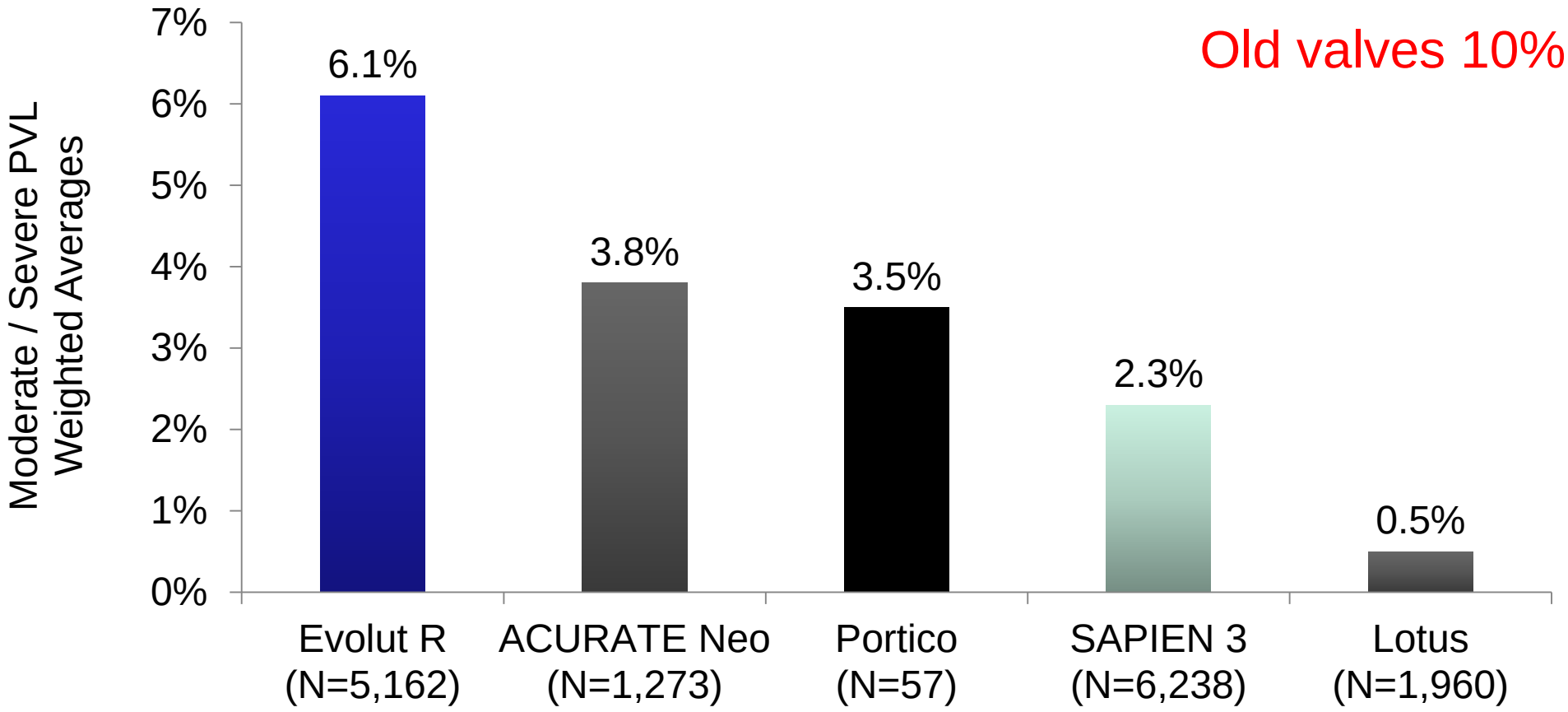
Major Vascular Complications have decreased substantially

Rates According to VARC 2

- Low profile delivery systems have enabled transfemoral TAVR in most patients



With newer valves we have seen lower rates of PVL



E. Grube, CRT 2017

New Aortic Valvuloplasty Balloons

More stable, lower risk of annulus rupture or providing continuous blood flow.

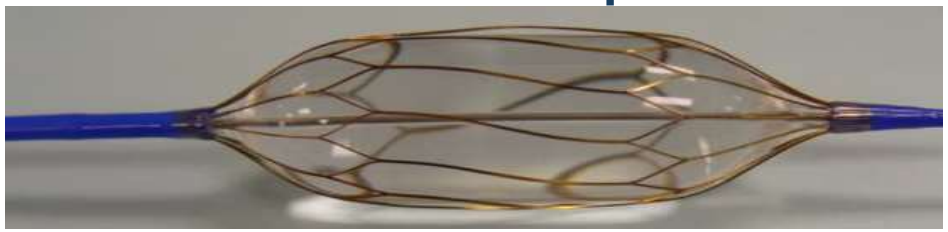
TRUE Balloon

Non-compliant and rupture resistant sizing

V8 Balloon

Locks into annulus for stability and reduced risk of annular rupture

CardioSculpt



Improve stability

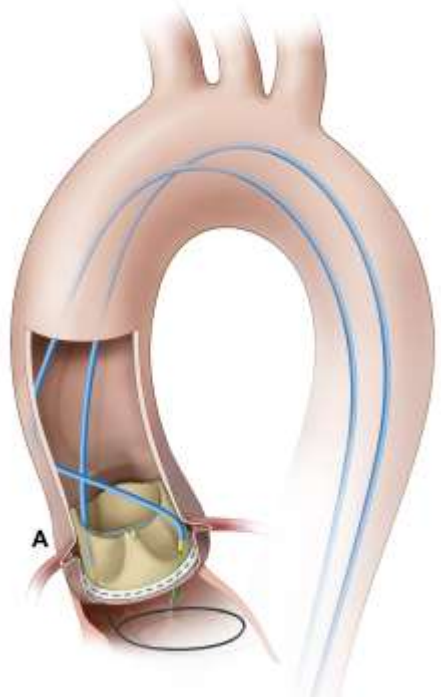
TRUE Flow Balloon

Provides continuous blood flow, rupture resistant

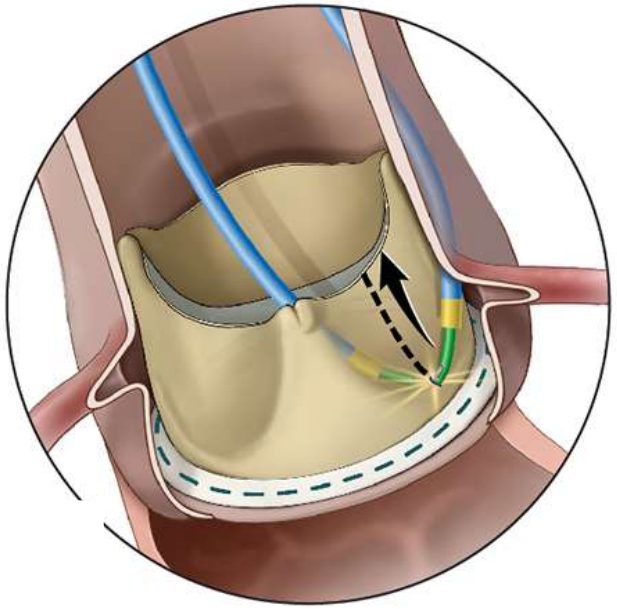
[1]Webb, presented at TCT 2015, [2]Woitek, presented at TCT 2017

BASILICA technique for valve in valve

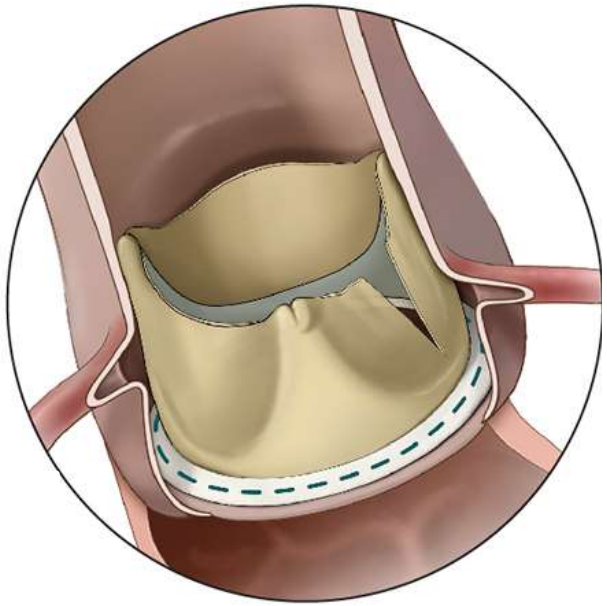
Reduces the risk of coronary obstruction post valve-in-valve



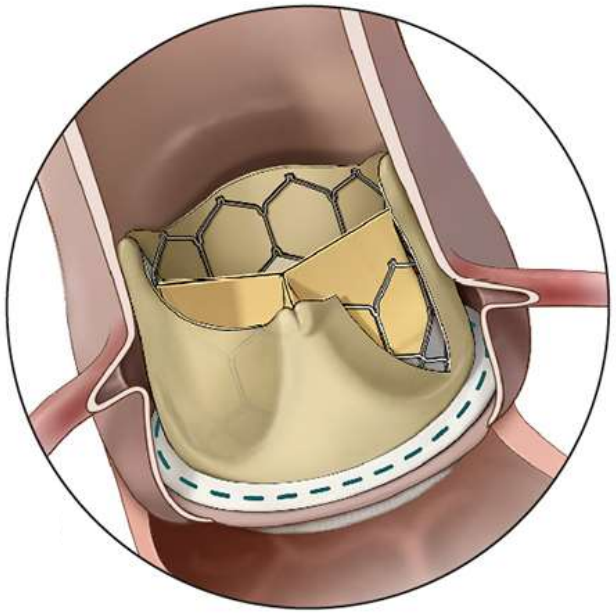
Leaflet wire traversal and snaring



Leaflet slicing



Sliced leaflet

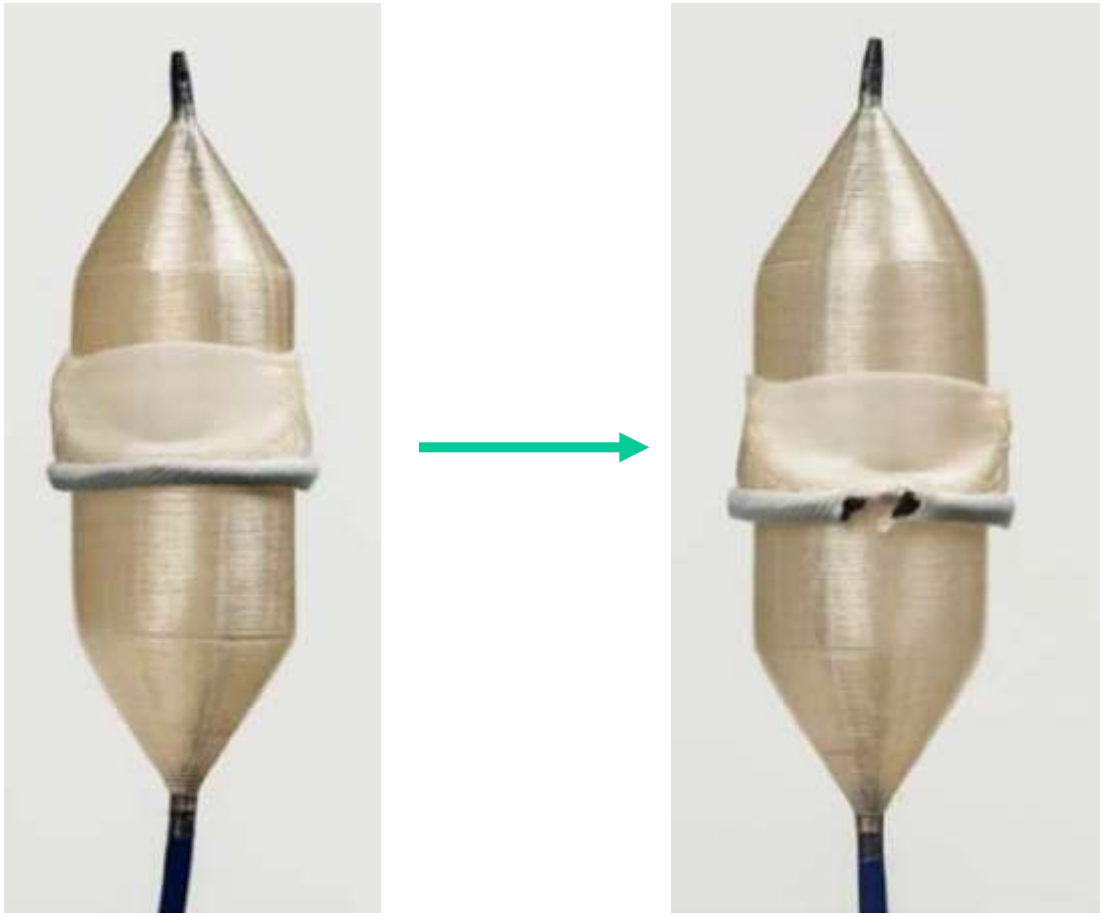


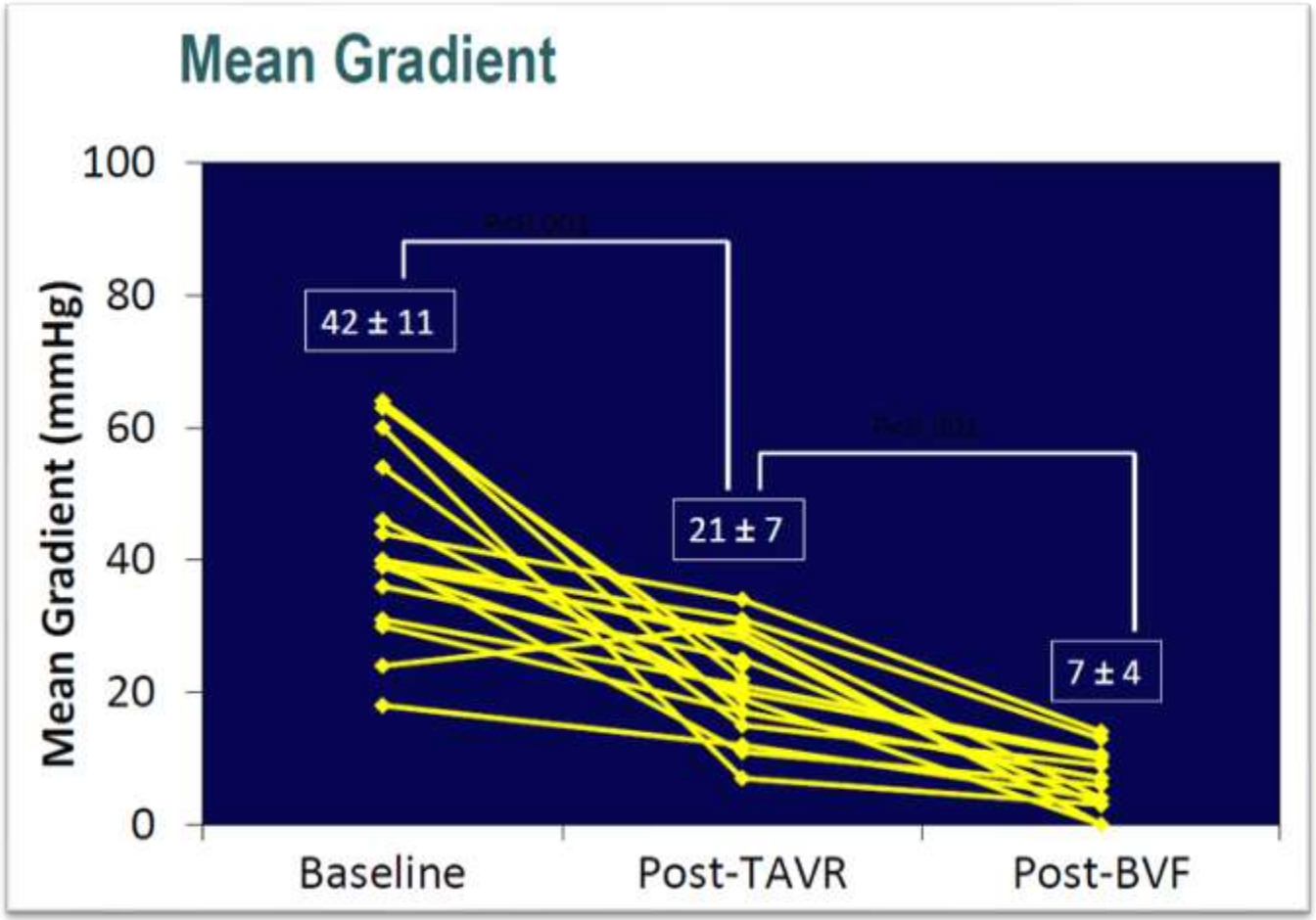
Valve-in-Valve

[1]Dvir, presented at TCT 2017

Valve Cracking for valve in valve procedures

A technique in patients with small valves to improve gradients post valve-in-valve procedure.





[1]Dvir, presented at ACC 2018

What does all this mean?

- After > 15 yrs, TAVR has become mature
- It is now the gold standard in high-, intermediate- and low-risk patients
- But we are not at the end of a development!
- We are still at the beginning
  - like PCI in the 90s!